

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:	)	
	)	
Xiangping Qian et al.	)	Group Art Unit: 1626
	)	
Application No.: 10/529,634	)	Examiner: Sun Jae Y. Loewe
	)	
Filed: November 16, 2005	)	
	)	
For: COMPOUNDS, COMPOSITIONS, AND METHODS	)	Confirmation No.: 1369

**MAIL STOP AMENDMENT**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**RESPONSE TO RESTRICTION REQUIREMENT AND AMENDMENT**

This Response to Restriction Requirement and Amendment is responsive to the Office Action mailed October 9, 2007. This reply is being filed on or before the current due date of November 9, 2007.

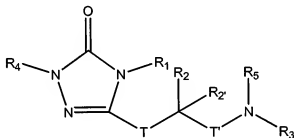
**Amendments to the Claims** begin on page 2 of this paper.

**Remarks** follow the amendments to the claims.

**AMENDMENT TO THE CLAIMS:**

This listing of claims replaces all prior versions and listings of claims in the application:

1. (Currently Amended) A compound selected from the group represented by Formula I:



Formula I

wherein:

T and T' are independently a covalent bond or optionally substituted lower alkylene;

R<sub>1</sub> is chosen from ~~hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;~~

R<sub>2</sub> and R<sub>2'</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; or R<sub>2</sub> and R<sub>2'</sub> taken together form an optionally substituted 3- to 7-membered ring;

R<sub>3</sub> is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, -C(O)-R<sub>6</sub>, and -S(O)<sub>2</sub>-R<sub>6a</sub>;

R<sub>4</sub> is independently chosen from hydrogen, optionally substituted alkyl,

carboxyalkyl, aminocarbonyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaralkyl, optionally substituted heterocyclyl and optionally substituted heteroaryl;

R<sub>5</sub> is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaralkyl-, and optionally substituted heterocyclyl-; [[or]]

or R<sub>5</sub> taken together with R<sub>3</sub>, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

or R<sub>5</sub> taken together with R<sub>2</sub> form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

R<sub>6</sub> is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, R<sub>7</sub>O- and R<sub>11</sub>-NH-;

R<sub>6a</sub> is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, and R<sub>11</sub>-NH-;

R<sub>7</sub> is chosen from optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; and

R<sub>11</sub> is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

and pharmaceutically acceptable salts thereof

~~a pharmaceutically acceptable salt of a compound of Formula I;~~

~~a pharmaceutically acceptable solvate of a compound of Formula I; or~~

~~a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I;~~

~~provided that R<sub>1</sub> is not optionally substituted phenyl when R<sub>4</sub> is optionally substituted phenyl.~~

2. (Currently Amended) The compound of Claim 1 comprising one or more of the following:

T and T' are absent;

R<sub>1</sub> is selected from ~~hydrogen, optionally substituted lower alkyl, optionally substituted benzyl~~[[,]] and optionally substituted naphthylmethyl, ~~and optionally substituted phenyl~~;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2</sub>' is hydrogen or optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted aryl, carbamyl, heteroaryl, or optionally substituted heterocycl;

R<sub>3</sub> is -C(O)R<sub>6</sub> or -SO<sub>2</sub>R<sub>6a</sub>;

R<sub>6</sub> is selected from optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl, optionally substituted aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R<sub>7</sub>O- and R<sub>11</sub>-NH-;

R<sub>6a</sub> is chosen from phenyl substituted with halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, cyano, nitro, methylenedioxy, or trifluoromethyl and naphthyl;

R<sub>7</sub> is chosen from optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl and optionally substituted aryl;

R<sub>11</sub> is chosen from hydrogen, optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl and optionally substituted aryl; and

R<sub>5</sub> is chosen from optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, and optionally substituted heteroaralkyl.

3. (Currently Amended) The compound of Claim 2 comprising one or more of the following:

R<sub>1</sub> is chosen from ~~hydrogen, ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl,~~

chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, tetrahydrofuranylmethyl, dichlorobenzyl, furanylmethyl, and dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R<sub>2</sub> is hydrogen;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is methyl, ethyl, propyl, phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, dihalophenyl-, pyridinyl, or benzyl;

R<sub>3</sub> is -C(O)R<sub>6</sub>;

R<sub>6</sub> is C<sub>1</sub>-C<sub>8</sub> alkyl, optionally substituted aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl, and optionally substituted aryl; and

R<sub>5</sub> is selected from optionally substituted alkyl, optionally substituted cyclohexyl; phenyl substituted with hydroxy, halogen, lower alkoxy or lower alkyl; benzyl; heteroaryl(methyl); heteroaryl(ethyl); and heteroaryl(propyl).

4. (Original) The compound of Claim 3 comprising one or more of the following:

R<sub>1</sub> is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R<sub>2</sub> is chosen from methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, and hydroxymethyl;

R<sub>2</sub> is hydrogen;

R<sub>4</sub> is phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, or dihalophenyl-;

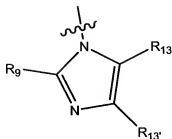
R<sub>6</sub> is tolyl, halophenyl, methylhalophenyl, hydroxymethylphenyl, methylenedioxyphenyl, formylphenyl, halo(trifluoromethyl)phenyl-, or cyanophenyl; and

R<sub>5</sub> is aminopropyl-; pyrrolidinylmethyl-; or piperidinylmethyl-.

5. (Original) The compound of Claim 1 comprising one or more of the following:

R<sub>1</sub> is benzyl;  
R<sub>2</sub> is hydrogen; and  
R<sub>2</sub> is ethyl or propyl.

6. (Previously amended) The compound of Claim 5 wherein R<sub>2</sub> is i-propyl.
7. (Currently Amended) The compound of Claim 1 comprising one or more of the following:
- T and T' are absent;
  - R<sub>1</sub> is selected from ~~hydrogen, optionally substituted lower alkyl, optionally substituted benzyl[[,]] and optionally substituted naphthylmethyl, and optionally substituted phenyl;~~
  - R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;
  - R<sub>2</sub> is hydrogen or optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;
  - R<sub>4</sub> is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted aryl, carbamyl, heteroaryl, or optionally substituted heterocyclyl;
  - R<sub>6</sub> is selected from optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl, optionally substituted aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R<sub>7</sub>O- and R<sub>11</sub>-NH-;
  - R<sub>7</sub> is chosen from optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl and optionally substituted aryl;
  - R<sub>11</sub> is chosen from hydrogen, optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl and optionally substituted aryl; and
  - R<sub>3</sub> taken together with R<sub>5</sub> and the nitrogen to which they are bound, forms an optionally substituted imidazoliny ring of the formula:



wherein

R<sub>9</sub> is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaralkyl, optionally substituted aralkoxy, optionally substituted heteroaralkoxy, and optionally substituted heteroaryl; and

R<sub>13</sub> and R<sub>13'</sub> are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, or optionally substituted aralkyl.

8. (Currently Amended) The compound of Claim 7 comprising one or more of the following:

R<sub>1</sub> is chosen from ~~hydrogen, ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, tetrahydrofuranylmethyl, dichlorobenzyl, furanylmethyl, and dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;~~

R<sub>2</sub> is hydrogen;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is methyl, ethyl, propyl, phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, dihalophenyl-, pyridinyl, or benzyl;

R<sub>6</sub> is C<sub>1</sub>-C<sub>8</sub> alkyl, optionally substituted aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl, and optionally substituted aryl;

and

R<sub>9</sub> is aryl, substituted aryl, aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, aralkoxy, heteroaralkoxy, substituted aralkyl, substituted heteroaralkyl, substituted aralkoxy, or substituted heteroaralkoxy.

9. (Currently Amended) The compound of Claim 1 comprising one or more of the following:

T and T' are absent;

R<sub>1</sub> is selected from ~~hydrogen, optionally substituted lower alkyl, optionally substituted benzyl[[,]] and optionally substituted naphthylmethyl, and optionally substituted phenyl;~~

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2'</sub> is hydrogen or optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted aryl, carbamyl, heteroaryl, or optionally substituted heterocyclyl;

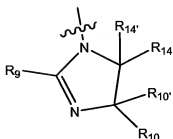
R<sub>6</sub> is selected from optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl, optionally substituted aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R<sub>7</sub>O- and R<sub>11</sub>-NH-;

R<sub>7</sub> is chosen from optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl and optionally substituted aryl;

R<sub>11</sub> is chosen from hydrogen, optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl and optionally substituted aryl; and

R<sub>3</sub> taken together with R<sub>5</sub> and the nitrogen to which they are bound, forms an optionally substituted imidazolyl ring of the formula:





wherein,

R<sub>9</sub> is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, optionally substituted aralkoxy, or optionally substituted heteroaralkoxy; and

R<sub>10</sub>, R<sub>10'</sub>, R<sub>14</sub>, and R<sub>14'</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, and optionally substituted aralkyl.

10. (Currently Amended) The compound of Claim 9 comprising one or more of the following:

R<sub>1</sub> is chosen from ~~hydrogen, ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, tetrahydrofuranylmethyl, dichlorobenzyl, furanylmethyl, and~~ dimethoxybenzyl, naphthylmethyl, and ~~(ethoxycarbonyl)ethyl~~;

R<sub>2</sub> is hydrogen;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is methyl, ethyl, propyl, phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, dihalophenyl-, pyridinyl, or benzyl;

R<sub>6</sub> is C<sub>1</sub>-C<sub>8</sub> alkyl, optionally substituted aryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl-C<sub>1</sub>-C<sub>4</sub>-alkyl-, optionally substituted heteroaryl, and optionally substituted aryl;

R<sub>8</sub> is aryl, substituted aryl, aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, aralkoxy, heteroaralkoxy, substituted aralkyl, substituted heteroaralkyl,

substituted aralkoxy, or substituted heteroaralkoxy;

R<sub>10</sub> is hydrogen or optionally substituted lower alkyl; and

R<sub>10'</sub> is hydrogen or optionally substituted lower alkyl.

11. (Original) The compound of Claim 1 wherein the stereogenic center to which R<sub>2</sub> and R<sub>2'</sub> is attached is of the R configuration.

12. (Original) The compound of Claim 1 wherein

T and T' are absent;

R<sub>1</sub> is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2'</sub> is hydrogen;

R<sub>4</sub> is phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, or dihalophenyl-;

R<sub>3</sub> is hydrogen; and

R<sub>5</sub> is hydrogen.

13. (Original) The compound of Claim 1 wherein

T and T' are absent;

R<sub>1</sub> is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2'</sub> is hydrogen;

R<sub>4</sub> is phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, or dihalophenyl-;

R<sub>3</sub> is -C(O)R<sub>6</sub>;

R<sub>5</sub> is selected from optionally substituted alkyl, optionally substituted cyclohexyl; phenyl substituted with hydroxyl, halogen, lower alkoxy or lower alkyl; benzyl; heteroaryl(methyl; heteroarylethyl; and heteroarylpropyl; and

R<sub>6</sub> is tolyl, halophenyl, methylhalophenyl, hydroxymethylphenyl, methylenedioxyphenyl, formylphenyl, halo(trifluoromethyl)phenyl-, or cyanophenyl.

14. (Currently Amended) The compound of Claim 1 wherein T and T' are absent;

R<sub>1</sub> is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2'</sub> is hydrogen;

R<sub>4</sub> is phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, or dihalophenyl-;

R<sub>3</sub> is -S(O)<sub>2</sub>-R<sub>6a</sub>-C(O)R<sub>6a</sub>;

R<sub>5</sub> is selected from optionally substituted alkyl, optionally substituted cyclohexyl; phenyl substituted with hydroxy, halogen, lower alkoxy or lower alkyl; benzyl; heteroarylmethyl; heteroarylethyl; and heteroarylphenyl; and

R<sub>6a</sub> is chosen from phenyl substituted with halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, cyano, nitro, methylenedioxy, or trifluoromethyl and naphthyl.

15. (Original) The compound of Claim 1 wherein T and T' are absent;

R<sub>1</sub> is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2'</sub> is hydrogen;

R<sub>4</sub> is phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, or dihalophenyl-; and

R<sub>5</sub> taken together with R<sub>3</sub> is an optionally substituted imidazolyl.

16. (Currently amended) The compound of Claim 1 wherein T and ~~T'~~ are T' are absent;

[[R<sub>1</sub>]] R<sub>1</sub> is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or

hydroxybenzyl;

R<sub>2</sub> is optionally substituted C<sub>1</sub>-C<sub>4</sub> C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2</sub> is hydrogen; and

R<sub>4</sub> is phenyl, halophenyl-, methylphenyl-, methoxyphenyl-, cyanophenyl-, trifluoromethylphenyl-, or dihalophenyl-;

R<sub>5</sub> taken together with R<sub>3</sub> is an optionally substituted imidazoliny.

17. (Previously amended) A pharmaceutical composition comprising a pharmaceutical excipient and a therapeutically effective amount of a compound of Claim 1.

18-21. (Cancelled).

## REMARKS

In a restriction requirement, mailed October 9, 2007, the Examiner required restriction between:

Group I: claims 1-17 and 21, drawn to products of Formula I and further election of a single compound; and

Group II: claims 18-20<sup>1</sup>, drawn to a process of using products of Formula I and a further election of a single compound.

Applicants elect, without traverse, Group I, claims 1-17 and 21, drawn to products of Formula I and the species of Example 2, i.e., the compound that is N-(3-amino-propyl)-N-[1-(4-benzyl-5-oxo-1-phenyl-4,5-dihydro-1H-[1,2,4]triazol-3-yl)-2-methyl-propyl]-4-methyl-benzamide. Claims 1-11, 13, and 17 are readable on the species.

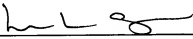
Applicants have cancelled the non-elected claims without prejudice to their prosecution in one or more continuing applications. Applicants have also made various amendments to the claims. Since all of these inventions are reasonably conveyed by the specification and original claims, there is no issue of new matter.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Date: November 9, 2007

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<sup>1</sup> The restriction requirement indicates that Group II includes claims 12 and 13. However, Applicants believe that the Office intended to reference claims 18-20, which are drawn to methods of using compounds of Formula I.